

NOVEL DRUGS APPROVED USING SURROGATE ENDPOINTS

January 1, 2010 - December 31, 2014

*In the last
five years,
FDA approved
197 novel
drugs and
biologics; 84
relied upon
surrogate
endpoints.*

Before the U.S. Food and Drug Administration (FDA) approves a drug or biologic, the product must show substantial evidence of effectiveness in clinical trials and that the benefits outweigh the risks. Clinical trials measure benefit using clinical endpoints, surrogate endpoints, or other types of measurements. Clinical endpoints measure how a patient feels or functions better, or lives longer. Surrogate endpoints are biomarkers, such as a laboratory test, radiographic image (e.g., x-rays, MRIs), and physical sign (e.g., blood pressure), that substitute for clinical endpoints in certain circumstances.

A surrogate endpoint may serve as the basis for traditional approval when it is known, through scientific study, to predict clinical benefit. A surrogate endpoint may serve as a basis for Accelerated Approval when it is reasonably likely to predict a drug's intended clinical benefit. Drugs approved under Accelerated Approval are subject to the requirement of post-approval confirmatory trials.

From 2010-2014, FDA approved 197 novel drugs, known as new molecular entities (NMEs), and New Biologic Approvals that include both New Drug Applications (NDAs) and Biologic License Applications (BLAs). The following table shows the 84 NME drugs and original biologics approved during that time period that relied upon a surrogate endpoint for an approval determination (i.e., traditional approval or Accelerated Approval). Many of these drugs have orphan designation, which means that they are intended to treat rare or uncommon diseases.

Approval Date	Drug Name	Abbreviated Indication*	Traditional Approval	Accelerated Approval**	Orphan Designation	Surrogate Endpoint
1/25/2010	Victoza (liraglutide)	Type 2 Diabetes Mellitus	✓			Hemoglobin A1C (HgA1C)
2/19/2010	Menveo	prevention of meningococcal A, C, Y, and W-135 infection	✓			Immunogenicity
2/24/2010	Prevnar13	prevention of invasive pneumococcal infection	✓			Immunogenicity
2/26/2010	Vpriv (velaglucerase alfa)	Type 1 Gaucher Disease	✓		✓	Hemoglobin (Hgb)
3/18/2010	Carbaglu (carglumic acid)	urea cycle disorder, N-acetylglutamate synthetase (NAGS) deficiency	✓		✓	Ammonia, glutamine, citrulline levels
5/24/2010	Lumizyme (alglucosidase alfa)	non-infantile onset Pompe disease (8 years and older)	✓		✓	Forced Vital Capacity (FVC) ***
6/1/2010	Prolia (denosumab)	osteoporosis	✓			vertebral fractures on xray
7/10/2010	Alpha-1-Proteinase Inhibitor (Human)	treatment of alpha-1-proteinase inhibitor deficiency	✓		✓	Protein levels
9/14/2010	Krystexxa (pegloticase)	gout	✓		✓	plasma uric acid level
11/10/2010	Egrifta (tesamorelin for injection)	Lipodystrophy in human immunodeficiency virus (HIV) patients	✓			percent change in visceral fat by computerized tomography (CT) scan
2/17/2011	Factor XIII Concentrate (Human)	prophylactic treatment of factor XIII deficiency		✓	✓	Pharmacokinetics
2/25/2011	Edarbi (azilsartan medoxomil)	hypertension	✓			Blood pressure (BP)
2/28/2011	Daliresp (roflumilast)	chronic obstructive pulmonary disease (COPD)	✓			Forced expiratory volume in 1 second (FEV1) ***
3/16/2011	Adenovirus Vaccine, Live, Oral Type 4 and Type 7	prevention of infection with two adenovirus types	✓			Immunogenicity (for Type 7)
4/6/2011	Caprelsa (vandetanib)	Medullary thyroid cancer	✓		✓	Progression Free Survival (PFS)
5/2/2011	Tradjenta (linagliptin)	Type 2 Diabetes Mellitus	✓			Hemoglobin A1C (HgA1C)
5/13/2011	Victrelis (boceprevir)	hepatitis C genotype 1	✓			Sustained Viral Response (SVR)

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5/20/2011	Edurant (rilpivirine)	human immunodeficiency virus (HIV)	✓			viral load
5/23/2011	Incivek (telaprevir)	hepatitis C genotype 1	✓			Sustained Viral Response (SVR)
6/15/2011	Nulojix (belatacept)	organ rejection prophylaxis	✓		✓	biopsy-proven acute rejection (BPAR)
7/1/2011	Arcapta Neohaler (indacaterol maleate)	chronic obstructive pulmonary disease (COPD)	✓			Forced expiratory volume in 1 second (FEV1)
8/19/2011	Adcetris (brentuximab vedotin)	1) Hodgkin's Lymphoma; 2) Systemic anaplastic large cell lymphoma		✓	✓	1) Overall objective response rate (ORR) using computerized tomography (CT) or positron emission tomography (PET) scans; 2) overall response rate (ORR)
8/26/2011	Xalkori (crizotinib)	non-small cell lung cancer (NSCLC), anaplastic lymphoma kinase (ALK) positive mutation		✓	✓	Objective response rate (ORR) using computerized tomography (CT) or magnetic resonance imaging (MRI)
10/14/2011	Feriprox (Deferiprone)	Transfusional iron overload due to thalassemia		✓	✓	serum ferritin
11/16/2011	Jakafi (ruxolitinib)	myelofibrosis	✓		✓	Percent reduction in spleen volume by computerized tomography (CT) or magnetic resonance imaging (MRI)
11/18/2011	Erwinaze (asparaginase erwinia chrysanthemi)	acute lymphoblastic leukemia (ALL)	✓		✓	trough asparaginase activity level
1/17/2012	Voraxaze (glucarpidase)	methotrexate (MTX) toxicity	✓		✓	plasma methotrexate (MTX) levels
1/27/2012	Inlyta (axitinib)	renal cell carcinoma (RCC)	✓			Progression Free Survival (PFS)
1/30/2012	Erivedge (vismodegib)	basal cell carcinoma	✓			Objective response rate (ORR)
1/31/2012	Kalydeco (ivacaftor)	cystic fibrosis, G551D mutation	✓		✓	Forced expiratory volume in 1 second (FEV1)
2/10/2012	Zioptan (tafluprost)	glaucoma	✓			intraocular pressure (IOP)
3/27/2012	Omontys (peginesatide)	anemia in chronic kidney disease	✓			Hemoglobin (Hgb)
5/1/2012	Elelyso (taliglucerase alfa)	Type 1 Gaucher Disease	✓		✓	spleen volume by magnetic resonance imaging (MRI)

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6/8/2012	Perjeta (pertuzumab)	HER-2 positive metastatic breast cancer	✓			Progression Free Survival (PFS)
6/14/2012	MenHibrix	prevention of meningococcal A and C and haemophilus influenzae B infection	✓			Immunogenicity
7/20/2012	Kyprolis (Carfilzomib)	multiple myeloma		✓	✓	Overall response rate (ORR) by International Myeloma Working Group (IMWG) criteria
7/23/2012	Tudorza Pressair (acclidinium bromide)	chronic obstructive pulmonary disease (COPD)	✓			Forced expiratory volume in 1 second (FEV1)
8/27/2012	Stribild (elvitegravir, cobicistat, emtricitabine, tenofovir disoproxil fumarate)	human immunodeficiency virus (HIV)	✓			viral load
8/29/2012	tbo-filgrastim	chemotherapy-induced neutropenia	✓			absolute neutrophil count (ANC)
9/4/2012	Bosulif (bosutinib)	chronic myelogenous leukemia (CML)	✓		✓	Major Cytogenetic Response (MCyR)
10/17/2012	Jetrea (ocriplasmin)	vitreal macular adhesion (VMA)	✓			Vitreomacular adhesion (VMA) by central reading
10/26/2012	Synribo (omacetaxine mepesuccinate)	chronic myelogenous leukemia (CML)		✓	✓	Major Hematologic Response (MaHR)
11/29/2012	Cometriq (Cabozantinib)	Medullary thyroid cancer	✓		✓	Progression Free Survival (PFS)
12/14/2012	Iclusig (ponatinib)	chronic myeloid leukemia (CML) and Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ALL)		✓	✓	Major Cytogenetic Response (MCyR) and Major Hematologic Response (MaHR)
12/14/2012	Signifor (pasireotide diaspertate)	Cushing's disease	✓		✓	urine free cortisol level
12/21/2012	Juxtapid (lomitapide)	homozygous familial hypercholesterolemia (HoFH)	✓		✓	Serum low-density lipoprotein-cholesterol (LDL-C)
12/28/2012	Sirturo (bedaquiline)	Multidrug resistant (MDR) pulmonary tuberculosis (TB)		✓	✓	time to sputum culture conversion

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1/25/2013	1) Nesina (alogliptin); 2) Oseno (alogliptin/pioglitazone); 3) Kazano (alogliptin/metformin)	Type 2 Diabetes Mellitus	✓			Hemoglobin A1C (HgA1C)
1/29/2013	Kynamro (mipomersen)	homozygous familial hypercholesterolemia (HoFH)	✓		✓	serum low-density lipoprotein-cholesterol (LDL-C)
2/8/2013	Pomalyst (pomalidomide)	multiple myeloma		✓	✓	Overall response rate (ORR) by European Group for Blood and Bone Marrow Transplant (EGBMT) criteria
2/22/2013	Kadcyla (ado-trastuzumab emtansine)	HER-2 positive metastatic breast cancer	✓			Progression Free Survival (PFS) using computerized tomography (CT) or magnetic resonance imaging (MRI) ***
2/26/2013	Osphena (ospemifene)	dyspareunia and/or vaginal dryness due to vulvar and vaginal atrophy	✓			parabasal and superficial cell maturation index on vaginal smear and vaginal pH***
3/29/2013	Invokana (canagliflozin)	Type 2 Diabetes Mellitus	✓			Hemoglobin A1C (HgA1C)
5/10/2013	Breo Ellipta (fluticasone furoate and vilanterol trifenate)	chronic obstructive pulmonary disease (COPD)	✓			Forced expiratory volume in 1 second (FEV1)
5/29/2013	Mekinist (trametinib)	unresectable or metastatic melanoma with BRAF V600E or V600K mutations	✓		✓	Progression Free Survival (PFS)
5/29/2013	Tafinlar (dabrafenib)	unresectable or metastatic melanoma with BRAF V600E or V600K mutations	✓		✓	Progression Free Survival (PFS)
7/12/2013	Gilotrif (afatinib)	NSCLC with epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations	✓		✓	Progression Free Survival (PFS)
8/12/2013	Tivicay (dolutegravir)	human immunodeficiency virus (HIV)	✓			viral load

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10/3/2013	Duavee (conjugated estrogens/bazedoxifene)	osteoporosis	✓			Bone marrow density (BMD) at lumbar (L)-spine
11/1/2013	Gazyva (obinutuzumab)	chronic lymphocytic leukemia (CLL)	✓		✓	Progression Free Survival (PFS)
11/13/2013	Imbruvica (ibrutinib)	mantle cell lymphoma (MCL)		✓	✓	Overall response rate (ORR)
11/22/2013	Olysio (simeprevir)	hepatitis C genotype 1	✓			Sustained Viral Response (SVR)
12/6/2013	Sovaldi (sofosbuvir)	hepatitis C genotypes 1, 2, 3 or 4	✓			Sustained Viral Response (SVR)
12/18/2013	Anoro Ellipta (umeclidinium and vilanterol)	chronic obstructive pulmonary disease (COPD)	✓			Forced expiratory volume in 1 second (FEV1)
1/8/2014	Farxiga (dapagliflozin)	Type 2 Diabetes Mellitus	✓			Hemoglobin A1C (HgA1C)
2/24/2014	Myalept (metreleptin)	leptin deficiency	✓		✓	Hemoglobin A1C (HgA1C)
4/15/2014	Tanzeum (albiglutide)	Type 2 Diabetes Mellitus	✓			Hemoglobin A1C (HgA1C)
4/23/2014	Sylvant (siltuximab)	multi-centric Castleman's disease (MCD) who are HIV and human herpes virus-8 (HHV-8) negative	✓		✓	Overall response rate (ORR)***
4/29/2014	Zykadia (ceritinib)	anaplastic lymphoma kinase (ALK) positive non-small cell lung cancer (NSCLC)		✓	✓	Overall response rate (ORR)
7/3/2014	Beleodaq (belinostat)	peripheral T-cell lymphoma (PTCL)		✓	✓	Overall response rate (ORR)
7/23/2014	Zydelig (idelalisib)	1) Chronic lymphocytic leukemia (CLL); 2) Follicular B-cell non-Hodgkin lymphoma (FL) and small lymphocytic lymphoma (SLL)	✓ ¹	✓ ²	✓	1) Progression Free Survival (PFS); 2) overall response rate (ORR)
7/31/2014	Striverdi Respimat (olodaterol)	Chronic obstructive pulmonary disease (COPD)	✓			Forced expiratory volume in 1 second (FEV1)

¹ for CLL indication

² for FL and SLL indications



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8/1/2014	Jardiance (empagliflozin)	Type 2 Diabetes Mellitus	✓			Hemoglobin A1C (HgA1C)
8/19/2014	Cerdelga (eliglustat)	Type 1 Gaucher Disease	✓		✓	spleen volume
9/4/2014	Keytruda (pembrolizumab)	unresectable or metastatic melanoma		✓	✓	tumor response rate by computerized tomography (CT) and magnetic resonance imaging (MRI)
9/18/2014	Trulicity (dulaglutide)	Type 2 Diabetes Mellitus	✓			Hemoglobin A1C (HgA1C)
10/10/2014	Harvoni (ledipasvir and sofosbuvir)	hepatitis C genotype 1	✓			Sustained Viral Response (SVR)
10/15/2014	Esbriet (pirfenidone)	idiopathic pulmonary fibrosis (IPF)	✓		✓	Forced Vital Capacity (FVC)
10/15/2014	Ofev (nintedanib)	idiopathic pulmonary fibrosis (IPF)	✓		✓	Forced Vital Capacity (FVC)
10/29/2014	Trumenba	prevention of meningococcal B infection		✓		Immunogenicity
12/3/2014	Blincyto (blinatumomab)	B-cell precursor acute lymphoblastic leukemia (ALL)		✓	✓	Complete remission (CR) or complete remission with partial hematological recovery (CRh)
12/19/2014	Viekira Pak (ombitasvir / paritaprevir / ritonavir / dasabuvir)	hepatitis C genotype 1	✓			Sustained Viral Response (SVR)
12/19/2014	Lynparza (olaparib)	advanced ovarian cancer with deleterious or suspected deleterious germline BRCA mutations		✓	✓	Objective response rate (ORR)
12/22/2014	Opdivo (nivolumab)	unresectable or metastatic melanoma		✓	✓	Objective response rate (ORR)

* Please see full indication in product labeling.

** There were 36 total Accelerated Approvals (AAs) for 2010-2014 including new and supplemental NDAs and BLAs as well as AAs based on intermediate clinical endpoints. 18 of those 36 AAs were for novel NME drugs and original biologics approved using surrogate endpoints—these are listed in the table.

*** Approval determination relied upon a surrogate endpoint and a direct clinical benefit; only the surrogate endpoint is listed in the table.

Please note: The information provided in the table is preliminary and should be considered a work-in-progress, as there is no established definition for “surrogate endpoint” vs. “clinical outcome assessment”.